Key challenges in device design and manufacturing

Dr. Orest Lastow
Medicon Valley Inhalation Consortium, MVIC AB

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Dr. Orest Lastow

- CEO Medicon Valley Inhalation Consortium, MVIC AB
- 15 years of inhalation experience from AstraZeneca
- Inventor and project manager of several inhalation projects
- Principal inventor of AstraZeneca new Dry Powder Inhalation platform
- Managed the AstraZeneca new DPI platform development programme for 6 years
MVIC is a full service CRO comprising 20 companies specializing in inhaled drug delivery.

We are about 60 inhalation experts, 25 with a PhD, representing over 800 years of inhalation experience.

MVIC has GMP facilities, well equipped labs, advanced instrumentation and highly skilled staff.

MVIC can offer a wide and comprehensive range of services and is a one-stop-shop for inhalation product development.
Challenge #1
Understanding the user
I want to feel safe and live my life
Perception

“My inhaler must be small and discrete”

“Why throw away something that looks so advanced”

“It looks very difficult to use”

“Is it environmentally friendly?”
“Should I inhale again, just to be sure?”

“Did my grandchild do it right?”

“How many doses do I have left?”

“Did I get my dose?”

“My life depends on this inhaler”
Use

“How do I clean it?”

“Can I use it without my glasses?”

“Does it fit my mouth?”

“How do I use my inhaler?”

“I hate fiddling with refills”

“Can I use it when my hands hurt?”
Conflicting needs
Challenge #2
Developing the device
Device development

**STEP 1**
Product definition
- Market analysis
- User studies
- Conceptual definition of DPI
- User requirement specifications, URS
- System requirement specifications, SRS
- Module requirement specifications, MRS
- Risk analysis

**STEP 2**
Concept Development
- Development of DPI modules
- Proof of principal testing
- Industrial design
- Engineering analysis
- 3D CAD
- Prototyping
- Test specifications
- Verification and performance testing using prototypes
- Risk analysis

**STEP 3**
Design freeze
- Selection of device supplier
- Selection of other suppliers
- Injection molded device (single cavity)
- Technical manufacturing of complete DPI
- Verification and performance testing using molded device
- User studies
- Documentation
- Risk analysis

**STEP 4**
Industrialization
- Design for manufacture and assembly
- Definition of manufacturing process
- Sourcing manufacturing equipment
- Sourcing semi automated assembly lines
- Sourcing GMP device (multiple cavities)
- Verification and performance testing using GMP device
- Risk analysis

**STEP 5**
Clinical supplies
- Validation of manufacturing equipment
- Stability testing
- GMP Manufacturing
- Manufacturing of clinical supplies
- Large scale GMP manufacturing
- Clinical trials
- Technology transfer

**STEP 6**
Commercial manufacturing
- Upgrading manufacturing equipment for commercial capacity or sourcing new commercial equipment
- Sourcing fully automated assembly lines
- File submission

**Key Deliverables**
- DPI specifications
- DPI concept prototypes verified
- Technical injection molded device verified
- GMP device and Phase III clinical trials capacity
- Clinical supplies
- Commercial manufacturing and first launch
## Formulation

- Module requirement specifications, MRS
- Identification of filler types
- Identification of available suppliers
- Feasibility studies with suppliers
- Test specifications
- Verification and performance testing using prototypes
- Selection of formulation
- Selection of process equipment
- Optimization of process parameters
- Supply of formulation for verification and performance testing
- Stability testing
- Toxicology studies

## Filling

- Module requirement specifications, MRS
- Identification of filler types
- Identification of available suppliers
- Feasibility studies with suppliers
- Test specifications
- Verification and performance testing using prototypes
- Selection of filler and supplier
- Verification and performance testing using molded device

## Device

- Market analysis
- User studies
- Conceptual definition of DPI
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- System requirement specifications, SRS
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- Risk analysis
- Development of DPI modules
- Proof of principal testing
- Industrial design
- Engineering analysis
- 3D CAD
- Prototyping
- Test specifications
- Verification and performance testing using prototypes
- Risk analysis
- Selection of device supplier
- Selection of other suppliers
- Injection molded device (single cavity)
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- User studies
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## Product definition

- Validation of manufacturing equipment
- Stability testing
- GMP Manufacturing
- Manufacturing of clinical supplies
- Large scale GMP manufacturing
- Clinical trials
- Technology transfer
- Upgrading manufacturing equipment for commercial capacity or sourcing new commercial equipment
- Sourcing fully automated assembly lines
- File submission
What could possibly go wrong?
What else can go wrong?
The team
The team

Chemistry

Pharmacy

Physics

Medicine

Engineering
Real connections
Traditional formulation development

Degradation
Compatibility
Solid state

Micronization
Mixing
GMP
Improved formulation development

- Degradation
- Compatibility
- Solid state
- Micronization
- Mixing
- GMP
- Process
- Filling
- Packaging
- Commercial manufacturing

- Absorption
- PK/PD

- Device interaction
- Modeling
- Electrostatics
Traditional device development

Design
Materials
Injection molding
Assembly
Improved device development

Polymer selection
Performance testing
Stability testing

Filling
Formulation
GMP

Design
Materials
Injection molding
Assembly

Lung deposition
In Vivo – In Vitro correlation

Device interaction
Aerodynamics
Modeling
Electrostatics
Is there more?
Wide tolerances
High Cpk
Cheap materials
Simple processes
Few parts

Tight tolerances
Advanced processes
High uniformity
Functional materials
Many functions
Challenge #3
Manufacturing the device
Technical liaison

- Help pharmacists and chemists to better understand engineers and vice versa
- Express pharmaceutical needs in engineering and manufacturing terms
- Match the pharmaceutical needs with manufacturers’ capabilities
- Provide a pharmaceutical perspective on tolerances, critical dimensions, mold design
- Identify appropriate level of quality at different development stages
- Strengthen interaction between R&D and Operations
- Help pharma company manage manufacturing suppliers
Manufacturing

Dos
• Supplier that understands the industry and inhaled products
• Clear and comprehensive specifications
• Agreed format and quality of the deliverables and how to verify
• Agreed price and what comes on top
• Agree on how to handle delays and revisions
• Always be the primary contact
• Visit supplier & make audits
• Pre-studies with more than one supplier
• Use suppliers to flush out the flaws
• Use a technical liaison

Don’ts
• Select a supplier without understanding the deliverables
• Suppliers making key decisions
• Consultants managing suppliers
• One supplier only
• Suppliers capability deciding the design
• Supplier selection when design is completed
• Obvious does not mean included
• Commit for to much at one time
• Believe that pharmacists and engineers speak the same language